"ANTI DIABETIC ACTIVITY OF PETROLIUM ETHER EXTRACT OF *TRIUMFETTA RHOMBOIDEA* ON STREPTOZOTOCIN INDUCED DIABETIC IN ALBINO RATS"

DEGREE DISSERTATION WORK SUBMITTED TO THE TAMILNADU Dr.M.G.R MEDICAL UNIVERSITY, CHENNAI IN PARTIAL FULFILLMENT FOR THE AWARD OF

MASTER OF PHARMACY

(PHARMACOLOGY)

Submitted by

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UNDER THE GUIDANCE OF

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Thesis Submitted to

The Tamilnadu Dr. M.G.R Medical University, Chennai

In partial fulfillment of the requirements

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APRIL 2014

CERTIFICATE

This is to certify that the dissertation entitled "Anti Diabetic activity of Petroleum ether Extract of *Triumfetta Rhomboidea* of streptozotocin induced Diabetic in albino mice" is a bonafide work done Mr.R.Padma Vinayaka Moorthy, R.V.S College of Pharmaceutical Sciences, Sulur, Coimbatore in partial fulfillment of the University rules and regulations for award of Master of Pharmacy in Pharmacology under my guidance and supervision during the academic year 2013-2014

Name and Signature of the Guide

Name and Signature of the Head of Department

Name and signature of the Dean

CERTIFICATE

This is to certify that the research work entitled **"Anti Diabetic activity of Petroleum ether extract of *Triumfetta rhomboidea* in Streptozotocin induced diabetic in albino rats"** submitted in partial fulfillment of the requirements for the award of Degree of **Master of Pharmacy** in **Pharmacology to the Tamilnadu Dr. M.G.R Medical University, Chennai** is a bonafide work carried out by **Mr.R.Padma Vinayaka Moorthy (Reg:261225657)** at the **Department of Pharmacology, R.V.S College Pharmaceutical Sciences Sulur, Coimbatore. 641402,**under my guidance and supervision during the academic year 2013-2014.

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(PADMA VINAYAGA MOORTHY.R)

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INTRODUCTION.

DIABETIC MELLITUS

Diabetic millets often referred to simply as diabetes (Ancient Greek: diabetes" to pass through [urine]") is a syndrome of disorder metabolism, usually due to a combination of hereditary and environment causes, resulting in abnormally high blood sugar level (hyperglycemia)

Diabetes is described as starvation in the midst of plenty. Because the body will have high amount of glucose level but the cells are incapable of consume it because of osmotic difference

Insulin is a hormone produced in the pancreas, which enable body cells to absorb glucose, to turn into energy. If the body cells cannot absorb the glucose, the glucose accumulates in the blood (hyperglycemia), leading to various potential medical complications.

TYPES OF DIABETES MELLITUS.

The type of diabetes is based on the presumed etiology they are

1. Type 1 diabètes or Insulin dependent diabetes mellitus (IDDM)
2. Type 2 diabètes or Non Insulin dependent diabetes mellitus (NIDDM)
3. Gestational Diabetes (Pregnancy diabetic).

1. TYPE 1 DIABETES

Insulin-dependent (Type I) diabetes mellitus is a chronic disease characterized by hyperglycemia, impaired metabolism and storage of important nutrients, evidence of autoimmunity, and long-term vascular and neurologic complications.

Insulin secretary function is limited. Cell membrane binding is not primarily involved. The goal of treatment is to relieve symptoms and to achieve blood glucose levels as close to normal as possible without severe hypoglycemia. However, even with education and self-monitoring of the blood glucose level, attaining recommended target values (plasma glucose level less than 8.0 mmol/L before main meals for adults) remains difficult.

. Therapy with one or two injections per day of mixed short-acting or intermediate-acting insulin preparations is a compromise between convenience and the potential for achieving target plasma glucose levels.

Intensive insulin therapy with multiple daily injections or continuous infusion with an insulin pump improves mean glycated hemoglobin levels; however, it increases rates of severe hypoglycemia and has not been shown to decrease the incidence of clinically significant renal, retinal or neurologic dysfunction. Future prospects include automated techniques of insulin delivery, immunosuppressant to preserve endogenous insulin secretion and islet transplantation.

Type 1 diabetes (IDDM) is characterized by loss of the insulin producing beta cells of the islet of Langerhans in the pancreas leading deficiency. In type 1 diabetes, the body does not produce insulin, and daily insulin injections are required. Type 1 diabetes is usually diagnosed during childhood or early adolescence and it affects about 1 in every 600 children.

It has two forms:

Immune Mediated Diabetes Mellitus**:** Results from a cellular mediated autoimmune destruction of the beta cells of the pancreas.

Idiopathic Diabetes Mellitus**:** Refer to forms of the disease that have unknown etiologies.

The majority of diabetes 1 is of the immune medicated in nature, where beta cells loss is a T cell mediated auto immune attack.

SYMPTOMS OF TYPE 1 DIABETIC

Type 1 diabetes signs and symptoms can come on quickly and may include:

- Increased thirst and frequent urination
- Extreme hunger
- Weight loss
- Fatigue
- Blurred vision

CAUSES OF TYPE 1 DIABETIC.

The exact cause of type 1 diabetes is unknown. In most people with type 1 diabetes, the body's own immune system which normally fights harmful bacteria and viruses mistakenly destroys the insulin-producing (islet) cells in the pancreas. Genetics may play a role in this process, and exposure to certain viruses may trigger the disease.

1) **A family history.** Anyone with a parent or sibling with type 1 diabetes has a slightly increased risk of developing the condition.

2) **Genetics.** The presence of certain genes indicates an increased risk of developing type 1 diabetes. In some cases — usually through a clinical trial genetic testing can be done to determine if someone who has a family history of type 1 diabetes is at increased risk of developing the condition.

3) **Geography.** The incidence of type 1 diabetes tends to increase as you travel away from the equator. People living in Finland and Sardinia have the highest incidence of type 1 diabetes — about two to three times higher than rates in the United States and 400 times that of people living in Venezuela

4) **Viral exposure.** Exposure to Epstein-Barr virus, coxsackievirus, mumps virus or cytomegalovirus may trigger the autoimmune destruction of the islet cells, or the virus may directly infect the islet cells.

5) **Early vitamin D.** Research suggests that vitamin D may be protective against type 1 diabetes. However, early drinking of cow's milk — a common source of vitamin D — has been linked to an increased risk of type 1 diabetes.

6) **Other dietary factors.** Omega-3 fatty acids may offer some protection against type 1 diabetes. Drinking water that contains nitrates may increase the risk. Consuming dairy products, particularly cow's milk, may increase infants' risk of the disease. Additionally, the timing of the introduction of cereal into a baby's diet may affect risk. One clinical trial found that between ages 3 and 7 months appears to be the optimal time for introducing cereal.

COMPLICATIONS OF TYPE 1 DIABETIC

Type 1 diabetes can affect major organs in your body, including heart, blood vessels, nerves, eyes and kidneys. Keeping the blood sugar level close to normal most of the time can dramatically reduce the risk of many complications.

Long-term complications of type 1 diabetes develop gradually, over years. The earlier you develop diabetes — and the less controlled your blood sugar the higher the risk of complications. Eventually, diabetes complications may be disabling or even life-threatening.

1) **Heart and blood vessel disease.** Diabetes dramatically increases your risk of various cardiovascular problems, including coronary artery disease with chest pain (angina), heart attack, stroke, narrowing of the arteries (atherosclerosis) and high blood pressure.

2) **Nerve damage (neuropathy).** Excess sugar can injure the walls of the tiny blood vessels (capillaries) that nourish your nerves, especially in the legs. This can cause tingling, numbness, burning or pain that usually begins at the tips of the toes or fingers and gradually spreads upward. Poorly controlled blood sugar could cause you to eventually lose all sense of feeling in the affected limbs. Damage to the nerves that affect the gastrointestinal tract can cause problems with nausea, vomiting, diarrhea or constipation. For men, erectile dysfunction may be an issue.

3) **Kidney damage (nephropathy).** The kidneys contain millions of tiny blood vessel clusters that filter waste from your blood. Diabetes can damage this delicate filtering system. Severe damage can lead to kidney failure or irreversible end-stage kidney disease, which requires dialysis or a kidney transplant.

4) **Eye damage.** Diabetes can damage the blood vessels of the retina (diabetic retinopathy), potentially leading to blindness. Diabetes also increases the risk of other serious vision conditions, such as cataracts and glaucoma.

5) **Foot damage.** Nerve damage in the feet or poor blood flow to the feet increases the risk of various foot complications. Left untreated, cuts and blisters can become serious infections. Severe damage might require toe, foot or even leg amputation.

6) **Skin and mouth conditions.** Diabetes may leave you more susceptible to skin problems, including bacterial and fungal infections. Gum infections also may be a concern, especially if you have a history of poor dental hygiene.

7) **Osteoporosis.** Diabetes may lead to lower than normal bone mineral density, increasing your risk of osteoporosis.

8) **Pregnancy complications.** High blood sugar levels can be dangerous for both the mother and the baby. The risk of miscarriage, stillbirth and birth defects are increased when diabetes isn't well controlled. For the mother, diabetes increases the risk of diabetic ketoacidosis, diabetic eye problems (retinopathy), pregnancy-induced high blood pressure and preeclampsia.

9) **Hearing problems.** Hearing impairments occur more often in people with diabetes.

TREATMENT FOR TYPE 1 DIABETES

- Exercising regularly and maintaining a healthy weight
- Eating healthy foods
- Monitoring blood sugar
- Taking insulin

The goal is to keep the blood sugar level as close to normal as possible to delay or prevent complications. Although there are exceptions, generally, the goal is to keep your daytime blood sugar levels before meals between **80 and 120 mg/dL** (4.4 to 6.7 mol/L) and your bedtime numbers between **100 and 140 mg/dL** (5.6 to 7.8 mol/L).

INSULIN

Insulin is a peptide hormone, produced by the beta cells of pancreas and is central to regulate the blood glucose level in the body. Patient with type 1 diabetic insulin cannot be secreted in their body (pancreas). So it (insulin) must be injected externally. Depends on their blood glucose level.

Table: 1-TYPES OF INSULIN

Each insulin has on own

Type of Insulin	Brand Name	Generic Name	Onset	Peak	Duration
Rapid-acting	NovoLog	Insulin aspart	15 minutes	30 to 90 minutes	3 to 5 hours
	Apidra	Insulin glulisine	15 minutes	30 to 90 minutes	3 to 5 hours
	Humalog	Insulin lispro	15 minutes	30 to 90 minutes	3 to 5 hours
Short-acting	Humulin R	Regular (R)	30 to 60 minutes	2 to 4 hours	5 to 8 hours
	Novolin R				
Intermediate-acting	Humulin N	NPH (N)	1 to 3 hours	8 hours	12 to 16 hours
	Novolin N				
Long-acting	Levemir	Insulin detemir	1 hour	Peakless	20 to 26 hours
	Lantus	Insulin glargine			
Pre-mixed NPH (intermediate-acting) and regular (short-acting)	Humulin 70/30 Novolin 70/30	70% NPH and 30% regular	30 to 60 minutes	Varies	10 to 16 hours
	Humulin 50/50	50% NPH and 50% regular	30 to 60 minutes	Varies	10 to 16 hours
Pre-mixed insulin lispro protamine suspension (intermediate-acting) and insulin lispro (rapid-acting	Humalog Mix 75/25	75% insulin lispro protamine and 25% insulin lispro	10 to 15 minutes	Varies	10 to 16 hours
	Humalog Mix 50/50	50% insulin lispro protamine and 50% insulin lispro	10 to 15 minutes	Varies	10 to 16 hours
Pre-mixed insulin aspart protamine suspension (intermediate-acting) and insulin aspart (rapid-acting)	NovoLog Mix 70/30	70% insulin aspart protamine and 30% insulin aspart	5 to 15 minutes	Varies	10 to 16 hours

- ✓ Peak
- ✓ Duration time.

- Onset is how soon the insulin starts a lower the blood glucose
- The peak is the time the insulin is working the hardest to lowering the blood glucose level.
- Duration is the time at how long the insulin lasts the length to keeps lowering the blood sugar

The chart shows the different insulin has different onset, duration and peak.

2. TYPE 2 DIABETES

Type 2 diabetes, once known as adult-onset or noninsulin-dependent diabetes, is a chronic condition that affects the way your body metabolizes sugar (glucose), your body's main source of fuel.

With type 2 diabetes, your body either resists the effects of insulin — a hormone that regulates the movement of sugar into your cells — or doesn't produce enough insulin to maintain a normal glucose level. Untreated, type 2 diabetes can be life-threatening.

It is the result of failure to produce sufficient insulin and insulin resistance. Elevated blood glucose levels are managed with reduced food intake, increased physical activity, and eventually oral medications or insulin

SYMPTOMS OF TYPE 2 DIABETES

Type 2 diabetes symptoms may develop slowly

1) Increased thirst and frequent urination

2) Increased hunger.

3) Weight loss.

4) Fatigue

5) Blurred vision.

6) Slow-healing sores or frequent infections.

CAUSES TYPE 2 DIABETES

1) **Weight.** Being overweight is a primary risk factor for type 2 diabetes. The more fatty tissue you have, the more resistant your cells become to insulin.

2) **Fat distribution.** If your body stores fat primarily in your abdomen, your risk of type 2 diabetes is greater than if your body stores fat elsewhere, such as your hips and thighs.

3) **Inactivity.** The less active you are, the greater your risk of type 2 diabetes. Physical activity helps you control your weight, uses up glucose as energy and makes your cells more sensitive to insulin.

4) **Family history.** The risk of type 2 diabetes increases if your parent or sibling has type 2 diabetes.

5) **Race.** Although it's unclear why, people of certain races — including blacks, Hispanics, American Indians and Asian-Americans — are more likely to develop type 2 diabetes than whites are.

6) **Age.** The risk of type 2 diabetes increases as you get older, especially after age 45. That's probably because people tend to exercise less, lose

muscle mass and gain weight as they age. But type 2 diabetes is also increasing dramatically among children, adolescents and younger adults.

7) **Prediabetes.** Prediabetes is a condition in which your blood sugar level is higher than normal, but not high enough to be classified as diabetes. Left untreated, prediabetes often progresses to type 2 diabetes.

COMPLAINTS TYPE 2 DIABETES

1) **Heart and blood vessel disease.** Diabetes dramatically increases the risk of various cardiovascular problems, including coronary artery disease with chest pain (angina), heart attack, stroke, narrowing of arteries (atherosclerosis) and high blood pressure. The risk of stroke is two to four times higher for people with diabetes, and the death rate from heart disease is two to four times higher for people with diabetes than for people without the disease, according to the American Heart Association.

2) **Alzheimer's disease.** Type 2 diabetes may increase the risk of Alzheimer's disease and vascular dementia. The poorer your blood sugar control, the greater the risk appears to be. So what connects the two conditions? One theory is that cardiovascular problems caused by diabetes could contribute to dementia by blocking blood flow to the brain or causing strokes. Other possibilities are that too much insulin in the blood leads to brain-damaging inflammation, or lack of insulin in the brain deprives brain cells of glucose.

3) **Nerve damage (neuropathy).** Excess sugar can injure the walls of the tiny blood vessels (capillaries) that nourish your nerves, especially in the legs. This can cause tingling, numbness, burning or pain that usu-

ally begins at the tips of the toes or fingers and gradually spreads upward. Poorly controlled blood sugar can eventually cause you to lose all sense of feeling in the affected limbs.

4) **Kidney damage (nephropathy).** The kidneys contain millions of tiny blood vessel clusters that filter waste from your blood. Diabetes can damage this delicate filtering system. Severe damage can lead to kidney failure or irreversible end-stage kidney disease, requiring dialysis or a kidney transplant.

5) **Foot damage.** Nerve damage in the feet or poor blood flow to the feet increases the risk of various foot complications. Left untreated, cuts and blisters can become serious infections. Severe damage might require toe, foot or even leg amputation.

6) **Skin and mouth conditions.** Diabetes may leave you more susceptible to skin problems, including bacterial and fungal infections. Gum infections also may be a concern, especially if you have a history of poor dental hygiene.

TREATMENT TYPE 2 DIABETES.

Diabetes mellitus type 2 is a chronic, progressive disease that has nl established cure, but does have well- established which can delay and sometimes which can delay and sometimes avoid most of the formerly inevitable of the condition.

They are two main goals of treatment.

- ✓ Reduction of morality and concomitant morbidity (from as-sorted diabetic complication
- ✓ Preservation of quality of life.

Oral hypoglycemic drugs are used to maintain the blood glucose level for some patient I have to take both oral drug and with insulin.

ORAL HYPOGLYCEMIC DRUGS.

a. **Sulphonyl ureas –**
    1. First generation
        i. Tolbutamide
        ii. Chlorpropamide
    2. Second generation
        i. Glibenglamide
        ii. Glipizide
        iii. Gliclazide and Glimiperide

b. **Biguanides**
    1. Metformin

c. Meglitinides
    a. Repaglinide
    b. Nateglinide

d. **Thiazolidine diones** –

a. Rosiglitazone
b. Pioglitazone

e. **Alpha glucosidase inhibitors**

Acarbose, Miglitol

Mechanism of action.

Sulfonylurea's bind to (K_{ATP}) channel on the cell membrane of pancreatic this inhibits a tonic, hyperpolarizing efflux of potassium, thus causing the electric potential over the membrane to become more positive. This opens voltage-gated channels. The rises in intracellular calcium leads to increased fusion of granulate with the cell membrane, and therefore increased secretion of (pro) insulin.

Tolbutamide

Tolbutamide is a first generation This drug may be used in the management of if diet alone is not effective. Tolbutamide stimulates the secretion of by the. Since the pancreas must synthesize insulin in order for this drug to work, it is not effective in the management of. It is not routinely used due to a higher incidence of adverse effects compared to newer second generation sulfonylurea's, such as it generally has a short duration of action due to its rapid metabolism, and is therefore safe for use in elderly diabetics.

Glimiperide.

The primary mechanism of action of glimepiride in lowering blood glucose appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells. In addition, extrapancreatic effects may also play a role in the activity of sulfonylureas such as glimepiride. This is supported by both preclinical and clinical studies demonstrating that glimepiride administration can lead to increased sensitivity of peripheral tissues to insulin. These findings are consistent with the results of a long-term, randomized, and

placebo-controlled trial in which AMARYL therapy improved postprandial insulin/C-peptide responses and overall glycemic control without producing clinically meaningful increases in fasting insulin/C-peptide levels. However, as with other sulfonylureas, the mechanism by which glimepiride lowers blood glucose during long-term administration has not been clearly established.

Glibenglamide.

The drug works by binding to and activating the regulatory subunit of the (K_{ATP}). This inhibition causes cell membrane opening. This results in an increase in intracellular in the and subsequent stimulation insulin release.

After a cerebral ischemic insult is broken and glibenclamide can reach the central nervous system. Glibenclamide has been shown to bind more efficiently to the ischemic hemisphere. Moreover, under ischemic conditions SUR1, the regulatory subunit of the K_{ATP-} and the NC_{Ca-ATP}-channels, is expressed in neurons, atrocities, oligodendrocytes, endothelial cells and by reactive microglia.

Gliclazide

Gliclazide selectively binds to sulfonylurea receptors on the surface of the pancreatic beta-cells. It was shown to provide cardiovascular protection as it does not bind to sulfonylurea receptors (n the heart This binding effectively closes the K+ ion channels. This decreases the efflux of potassium from the cell which leads to the depolarization of the cell. This causes voltage dependent Ca+ + ion channels to open increasing the Ca++ influx. The calcium can then bind to and activate calmodulin which in turn leads to exocytose of insulin vesicles leading to insulin release

Metformin

Metformin activates AMP activated protein kinase (AMPK) a liver enzyme that play an important role in signaling whole body energy balance and the glucose and fats activation of AMPK is required for Metformin inhibitory effects on the production of liver glucose.

Repaglinide.

Repaglinide acts by stimulating release of insulin from the cells of the islets of pancreas inhibiting ATP-sensitive K+ channels, thereby activating the Ca++ channels with increase in intracellular calcium to release insulin. However, repaglinide acts on a different binding site than the sulphonylureas. Repaglinide is not effective in the absence of functioning beta-cells. Repaglinide increases the amount of insulin released in a natural and physiological pulsatile pattern the activity of repaglinide is dose-dependent. Mean insulin levels begin to rise approximately 1.5 hours after the pre-prandial dose of repaglinide and declines towards baseline levels between meal-time the rapid onset of action and the short duration of hypoglycemic effect of repaglinide makes this agent suitable for pre-prandial administration. The main advantage of pre-prandial administration is that patients can miss or postpone a meal (and the corresponding repaglinide dose) without increasing the risk of hypoglycemia or compromising glycaemic control.

Pioglitazone.

Pioglitazone is an oral drug that reduces the amount of glucose (sugar) in the blood. It is in a class of anti-diabetic drugs called thiazolidinediones that are used in the treatment .The other member in this class is . (Another member of this class, troglitazone or Rezulin, was removed from the market because of .) Patients with type 2 diabetes cannot make enough insulin, and the cells of their body respond less to the insulin that is produced. Since insulin is the hormone that stimulates cells to remove glucose from the blood, the reduced amount of insulin and its reduced effect cause cells to take up less glucose from the blood and the level of glucose in the blood to rise. Pioglitazone often is referred to as an "insulin sensitizer" because it attaches to the insulin receptors on cells throughout the body and causes the cells to become more sensitive (more responsive) to insulin. As a result, more glucose is removed from the blood, and the level of glucose in the blood falls. At least some insulin must be produced

by the pancreas in order for pioglitazone to work. Pioglitazone also lowers the level of glucose in the blood by reducing the production and secretion of glucose into the blood by the liver. In addition, pioglitazone may alter the blood concentrations of lipids (fats) in the blood. Specifically, it decreases and increases the "good" (HDL)

Acarbose.

Acarbose inhibits enzymes, specifically, enzymes in the brush border of the small intestines and pancreatic alpha-amylase hydrolyzes complex starches to in the lumen of the small intestine, whereas the membrane-bound intestinal alpha-glucosidase in the small intestine. Inhibition of these enzyme systems reduces the rate of digestion of complex carbohydrates. Less glucose is absorbed because the carbohydrates are not broken down into glucose molecule.

III) GESTATIONAL DIABETES

This type affects females during pregnancy. Some women have very high levels of glucose in their blood, and their bodies are unable to produce enough insulin to transport all of the glucose into their cells, resulting in progressively rising levels of glucose. Diagnosis of gestational diabetes is made during pregnancy.

The majority of gestational diabetes patients can control their diabetes with exercise and diet. Between 10% to 20% of them will need to take some kind of blood-glucose-controlling medications. Undiagnosed or uncontrolled gestational diabetes can raise the risk of complications during childbirth. The baby may be bigger than he/she should be.

COMPLICATIONS GESTATIONAL DIABETES

i. Increased risk of prenatal mortality and morbidity.

ii. Obesity or impaired glucose intolerance in the offspring accompanied by macrosomia

iii. Neural tube defects

iv. Prematurity syndromes

CAUSES GESTATIONAL DIABETES.

Age > 30 years, obesity (BMI > 27.3 kg/m2), family history of diabetes, glycosuria, previous macrosomia, previous congenital malformation, previous stillbirth, past history of Gestational diabetes mellitus.

TESTES FOR DIABETIC

- **Glycated hemoglobin (HbA1C) test.** This blood test indicates your average blood. The term HbA1c refers to Glycated hemoglobin. It develops when hemoglobin a protein within red blood cells that carrier's oxygen throughout the body. Joins in the blood becomes "Glycated" by measuring Glycated hemoglobin (HbA1c), clinicians are able to get an overall picture of what is the average blood sugar level have been over a period of week or month

- .**Random blood sugar test.** A blood sample will be taken at a random time. Blood sugar values are expressed in milligrams per deciliter (mg/dL) or mill moles per liter (mmol/L). Regardless of when you last ate, a random blood sugar level of 200 mg/dL (11.1 mmol/L) or higher suggests diabetes, especially when coupled with any of the signs and symptoms of diabetes, such as frequent urination and extreme thirst.

- **Fasting blood sugar test.** A blood sample will be taken after an overnight fast. A fasting blood sugar level less than 100 mg/dL (5.6 mmol/L) is normal. A fasting blood sugar level from 100 to 125 mg/dL

(5.6 to 6.9 mmol/L) is considered prediabetes. If it's 126 mg/dL (7 mmol/L) or higher on two separate tests, you have diabetes.

DIABETIC INDUCED BY STREPTOZOTOCIN.

Streptozotocin is a toxic glucose analogue that preferentially accumulates in pancreatic beta cells via the GLUT2 glucose transporter. Especially the Streptozotocin inhibits insulin secretion and causes a state of insulin dependent diabetes mellitus. Both effects can be attributed to its specific chemical properties, namely its alkylating potency as with Streptozotocin its beta cell specificity is mainly the result of selective cellular uptake and accumulation.

Beta cells selectivity of Streptozotocin

Streptozotocin is a nitrosourea analogue in which the *N* methyl *N* *nitrosourea* (MNU) moiety is linked to the carbon 2 of a hexose. The action of Streptozotocin and chemically related alkylating compounds requires their uptake into the cells. Nitrosourea are usually lipophilic and tissue uptake to a plasma membrane in rapid; hour as a result of the hexose substitution,

Streptozotocin is less lipophilic. Streptozotocin is selectively accumulated in pancreatic β cells via the low- affinity GLUT2 glucose transporter in the plasma membrane. Thus, insulin-producing cells they do not express this glucose transporter are resistant to Streptozotocin. This observation also explains the greater toxicity of Streptozotocin compared with N- methyl-N-nitrosourea in cells that express GLUT2, even though both substances alkylating DNA to a similar extent. The importance of the GLUT2 glucose transporter in this process is also shown by the observation that Streptozotocin damages other organs expressing this transporter, particularly kidney and liver.

β cells toxicity

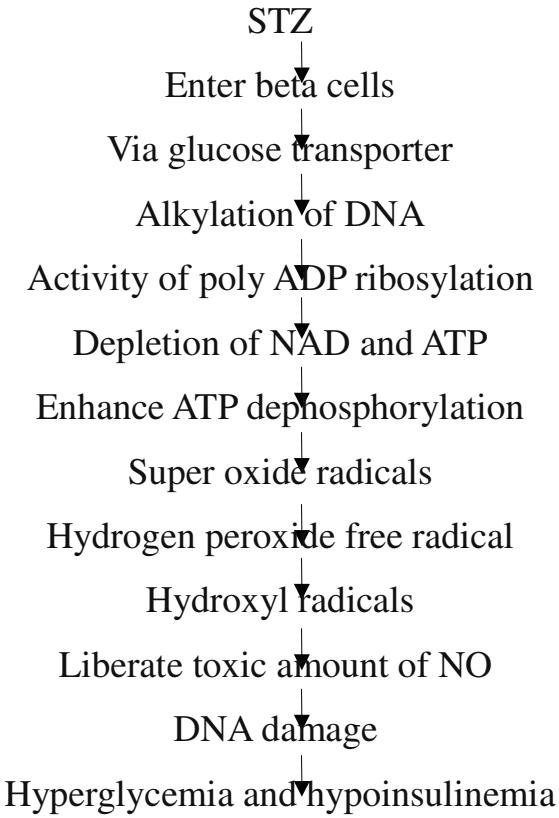
It is generally assumed that the toxicity of Streptozotocin is dependent up on the DNA alkylating activity of this methylnitrosourea moiety especially at the 6 position of guanine. The transfer of the methyl group Streptozotocin DNA molecules causes damage, which along a define chain of events, results in the fragmentation of the DNA. Protein glycosylation may be an additional damaging factor. In the attempt to repair DNA polymerase is over stimulated. This diminishes cellar NAD+ and subsequently ATP Ultimately responsible for beta cell death, but it is likely that protein methylation contributed to the functional defects of the beta cells after exposure to Streptozotocin

Inhibition of insulin secretion by Streptozotocin

The effects of Streptozotocin on glucose and insulin homeostasis reflect the toxin induced abnormalities in beta cell function. Initially biosynthesis, glucose induced insulin secretion and glucose metabolism is all affected. On the other hand Streptozotocin has no immediate direct inhibitory effect upon glucose transport or upon glucose stage of transport or upon glucose phosphorylation by glucokinase. However at later stages of functional beta cells impairment deficiencies in teams of gene expression and protein production lead to the deterioration of both glucose transport and metabolism

Even before the negative effect of mitochondrial DNA and protein alkylation and glycosylation become evident Streptozotocin induced depletion of NAD may result in the inhibition of insulin biosynthesis and secretion later inhibition of glucose induced and amino acid induced insulin secretion as a result of mitochondrial genome become apparent. This impairment is more marked for nutrient that for non nutrient insulin secretion. This interpretation has been confirmed through studies which have shown that pre treatment of isolated pancreatic islet with polymerase inhibitor nicotinamide prevents early inhibition of beta cells function beta cell function during first day after Streptozotocin exposure while long term inhibition of insulin secretion 6 days after Streptozotocin exposure

MECHANISM OF ACTION OF STREPTOZOTOCIN.



HERBAL MEDICINE TODAY

In recent years, there has been renewed interest in the treatment against different diseases using herbal drugs as they are generally non-toxic and World Health Organization has also recommended the evaluation of the effectiveness of plants in condition where we lack safe modern drugs. Plant derivatives with hypoglycemic properties have been used in folk medicine and traditional healing systems around the world from very ancient time. Despite the introduction of hypoglycemic agents from natural and synthetic sources, diabetes and its secondary complications continue to be a major medical problem to people (Ravi et al., 2005). Medicinal plants used to treat hypoglycemic and hyperglycemic conditions are of considerable interest to ethno botanical community as they are recognized to contain valuable medicinal properties in different parts of the plant.

In traditional medicine diabetes mellitus is treated with diet, physical exercise and medicinal plants, even though, more than 1200 plants are used around the world in the control of diabetes mellitus and approximately 30% of the traditionally used ant diabetic plants were pharmacologically and chemically investigated (Alarcon-Aguilar et al., 2002). On the other hand, potential hypoglycemic agents have also been detected for more than 100 plants used in ant diabetic therapy. Traditional treatments may provide the valuable clues for the development of new oral hypoglycemic agents and simple dietary adjuncts. More than 100 medicinal plants are mentioned in the Indian system of medicines including folk medicines for the management of diabetes, which are effective either separately or in combinations

LITERATURE REVIEW

Sivakumar.P et al (2001) was investigated the anti tumor activity of the triumfetta rhomboidea in the methanol extract in the albino mice. The METR administrated at the doses of 100, 200 and 400 mg/kg of the plant extract in mice bearing for 14 days after 24 hours of the tumor induction. The effects of METR on the growth of the marine tumor, life span of EAC bearing mice were also estimated treatment with METR brought back the hematological parameter more or less normal level. We have performed molecular dynamics (MD) simulation and Concord calculation on the LOV2 domain of triumfetta rhomboidea with the goal of detect possible superoxide dismutase (SOD) and Catalase (CAT). The present work indicates that the methanol extract of triumfetta rhomboidea exhibited significant of antitumor and antioxidant activity in vivo

K.P.Lissy*et.al.(2006) was investigated the ANTIOXIDANT POTENTIAL of triumfetta rhomboidea (root) they were collected the methanolic extract of the plant leafs. From that they have been prepared the dose of 100mg/kg, 200mg/kg and 400mg/kg and thus have been studied by using Wistar mice. The cancer has been introduced to the animal the maximum activity of the extract has been achieved by the methanolic extract of the plant leafs

Muhammad Iqbal et al (2010) Coal-smoke emissions affected photosynthesis, N-metabolism and growth characteristics of Triumfetta rhomboidea, as observed at pre-flowering, flowering and post-flowering stages of plant growth. The netphotosynthetic rate and stomata conductance decreased, whereas intercellular CO2 concentration increase dander pollution stress. The amounts of photosynthetic pigments in leaves were consistently less, up to 35% for chlorophylls and 84% for carotenoids. Nitrate level was raised while NR activity and protein contents in leaves declined at the polluted site at each growth stage. Sugar content was always lower at the polluted site in roots and stem but sizably higher in leaves, thus showing a failure of the process of

photosynthetic translocation. The sulphur level in roots, stem and leaves increased consistently. The leaf area was conspicuously reduced, leading to a significant loss in the total photosynthetic surface, despite an increase in the stem length and the

Ghodosara V.P et.al(2010) was proofed the the anti bacterial activity of the ethanolic extract of the *triumfetta rhomboidea.* the ethanolic activity of the extract is investigated in the albino mice it may gives positive Knollar's and Libermann Burchred test and the colour produced was typical of triterpences. The IR spectrum produced similar to triteropences, IR spectrum in the fundamental region also supported triterpense structure as the bands were noticed due to O H stretching.

Z naturforsh C et. Al (2003) was studied the mechanism of signal transduction from the LOV domain toward the kinase region of phototropin os still not well understood. We have performed molecular dynamics (MD) simulation and Concord calculation on the LOV2 domain of triumfetta rhomboidea with the goal of detect possible difference between the two forms of the LOV domain which may nit show up in the static crystal structure. Since no such clear difference are found in the MD simulations also, we suggested that the real biologically active conformation of the LOV domain within the whole phototropin

H.Neef et al (1996) was reported NINE European plants were selected to br screned for hypoglycemic activity. Selection criteria were based on traditional use and litreture reference. have been studied by using Wistar mice. The cancer has been introduced to the animal the maximum Total extracts of the plants were prepares by boiling the dreid materials with water or macerating it with 80% ethanol. Male swiss mice were orally loaded with glucose after the extract had been given by oral gavage.

John et al (2010) The methanolic extract of Sida retusa Linn. (Malvaceae),Urena lobata Linn.(Malvaceae)and Triumfetta rhomboidea Jacq.

(Teliaceae) roots were found to inhibit lipid peroxidation, scavenge hydroxyl and superoxide radicals in vitro. The quantity of S.retusa root extract required for 50% inhibition of lipid peroxidation, scavenging hydroxyl radical and superoxide radical was 1130.24 ug/ml respectively. IC 50 of root extract of U.lobata was 470.60 ug/ml, 1627.35ug/ml and 1109.24 ug/ml for superoxide radical scavenging, hydroxyl radical scavenging and lipid peroxidation respectively. T.rhomboidea root extract required for IC 50 was 336.65 ug/ml, 1346.03 ug/ml and 1004.22 ug/ml for superoxide scavenging, hydroxyl radical scavenging and lipid peroxidation respectively. The present investigation indicated that S. retusa, U.lobata ajaThe methanolic extract of Sida retusa Linn. (Malvaceae),Urena lobata Linn.(Malvaceae)and Triumfetta rhomboidea Jacq. (Teliaceae) roots were found to inhibit lipid peroxidation, scavenge hydroxyl and superoxide radicals in vitro. The quantity of S.retusa root extract required for 50% inhibition of lipid peroxidation, scavenging hydroxyl radical and superoxide radical was 1130.24 ug/ml respectively. IC 50 of root extract of U.lobata was 470.60 ug/ml, 1627.35ug/ml and 1109.24 ug/ml for superoxide radical scavenging, hydroxyl radical scavenging and lipid peroxidation respectively. T.rhomboidea root extract required for IC 50 was 336.65 ug/ml, 1346.03 ug/ml and 1004.22 ug/ml for superoxide scavenging, hydroxyl radical scavenging and lipid peroxidation respectively.

Jayankar et al (2010) was investated experimentally the possible antitumor effect and antioxidant role of methanol extract of Triumfetta rhomboidea (METR) leaves against Ehrlich ascites carcinoma (EAC) bearing Swiss albino mice. The METR administered at the doses of 100, 200 mg/kg, in mice for 14 days after 24 hours of tumor inoculation. The effects of METR on the growth of murine tumor, life span of EAC bearing mice were studied. Hematological profile and liver biochemical parameters (lipid peroxidation, antioxidant enzymes) were also estimated. Treatment with METR decreased the tumor volume and viable cell count there by increasing the life span of EAC bearing

mice. METR brought back the hematological parameter more or less normal level. The effect of METR also decreases the levels of lipid peroxidation and increased the levels of glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT). The present work indicates that the methanol extract of Triumfetta rhomboidea exhibited significant antitumor and antioxidant activity in vivo.

PLANT PROFILE

. . . Triumfetta rhomboidea . . .

PLANT PROFILE

Rank		Scientific Name and Common Name
Kingdom	-	Plantae – Plants
Subkingdom	-	Trachebionta – Vascular plants
Super division	-	Spermatophyte- Seed plant
Division	-	Magnoliphyta-Flowering plant
Class	-	Magnoliopsida – Dicotyledons
Subclass	-	Dillenilidae.
Order	-	Malvales.
Family	-	Tilianceae – Linden family.
Genus	-	*Triumfetta* L.burbark.
Species	-	*Triumfetta rhomboidea Jacq. – Diamond burbark.*

Vernacular names:

English - Chinese Burr, Burr Bush, Diamond Burrbark.

Tamil - Ottu Pullu.

Hindi - Chiriyari.

Telugu - Bankathuthara

Kannada - Kadu bende.

Botanical Name

Triumfetta rhomboidea.

Family

Tiliaceae (phalsa family)

Description.

It is an erect woody herb or shrub 75- 150 cm in height. Stems glabrous longitudinally grooved. Leaves simple, alternate; blade ovate to rhomboid in shape with 3-5 lobes, sometimes nearly as wide as broad and 2-10 cm long. Leaf margins irregularly serrate leaf surface softly pubescent with satellite hairs, blade palmately veined. Flowers small yellow clustered on the leafs axils. Five yellow, obviate petals about 5 mm long. Stamens 10-15, Fruits a subglobose bur with the body 3-4 mm in diameter, covered with 75-100 hooked spines 1.0 to 1.5

Part Used : Leafs.

AIM AND OBJECTIVE.

It is divided into following phase-

PHASE I : Taxonomical studies.

- ✓ Collection of plants.
- ✓ Authentication of plants.
- ✓ Powdered the leafs.

PHASE II : Pharmacognostical studies.

- ✓ Successively solvent Extraction.
  - Alcohol (ethanol).
  - Petroleum ether.
  - Benzene
  - Water.
- ✓ Preliminary Phytochemistry screenings.
  - Alkaloids
  - Saponins.
  - Tannins
  - Amino acid
  - Flavonoids
  - Terpenoids
  - Protein
  - Steroids

PHASE III : **Pharmacological studies.**

- ✓ Acute toxicity studies (as per OECD guidelines)
- ✓ Induction of diabetic animal
- ✓ Induces diabetic in rats by STZ
- ✓ Measuring the body weight
- ✓ Measuring the serum glucose level
- ✓ Measuring the plasma glucose
- ✓ Determination of lipids
    - o Triglyceride
    - o Total cholesterol
    - o HDL
    - o VLDL

PHASE IV : **Result and Documentation.**

Evolution of statistical significance result by computer aided program and systemic documentation. Values were presented as mean SEM Data were analyzed using of variance (ANOVA) and group means were compared with Turkey's post hoc Multiple Comparison Test using prism software version 5.

$P<0.05$ is considered as significant.

Plan of work

Literature review

Selection of plant

Collection of plant

Authentication of plant

Powdered the leafs

Extraction of powered plant leafs

Phytochemical Screening

Screening

- Alkaloids
- Saponins
- Tannins
- Flavonoids
- Terpeniods
- Proteins etc.,

Pharmacological

Acute toxicity studies

Diabetic induced by STZ

Measuring serum glucose

Measuring body weight

Determination of lipids

Result and discussion

Conclusion

MATERIALS AND METHOD.

TAXONOMICAL STUDIES.

1) **Collection of plants.**

Triumfetta rhomboidea was produced from the Botany Central council for Research in Ayurvedia and Siddha Govt of India.

The freshly collected sample were thoroughly cleaned and soaked in fresh water repeatedly to separate mud particles sticking on to plant constituents. The plants constituents collected were cut into small bits of about 2-3 in size. Then the leafs of the plants are powdered with a mechanical grinder. This powder was subjected to various studies for which the materials and methods which is presented below.

2) Authentication of plant.

The dried whole plant powder of triumfetta rhomboidea was supplied and authenticated by Chelladurai.v research officer Botany Central council for Research in Ayurvedia and Siddha Govt of India.

Pharmacognostical studies.

Extraction procedure.

Equal amount of the weighed powder were mixed and placed in the Soxhlet apparatus by using various solvents.

- Petroleum ether.
- Chloroform.
- Alcohol (ethanol).
- Benzene

- **Petroleum ether extraction.**

From the 500gm of crude powder was extracted with 2.5 liter of Petroleum ether (60 – 80) by continuous hot percolation using Soxhlet apparatus. This can be continued up to 24 hours.

Now the solvent petroleum ether was extracted out and filtered and the Soxhlet is removed the obtained residue is stored in the dissector.

- **Chloroform extraction.**

From the 500gm of crude powder was extracted with 2.5 liter of chloroform (60 – 80) by continuous hot percolation using Soxhlet apparatus. This can be continued up to 24 hours.

Now the solvent petroleum ether was extracted out and filtered and the Soxhlet is removed the obtained residue is stored in the dissector.

- **Alcohol extraction (ethanol)**

From the 500gm of crude powder was extracted with 2.5 liter of ethanol (60 – 80) by continuous hot percolation using Soxhlet apparatus. This can be continued up to 24 hours.

Now the solvent petroleum ether was extracted out and filtered and the Soxhlet is removed the obtained residue is stored in the dissector.

- **Benzene extraction**

From the 500gm of crude powder was extracted with 2.5 liter of benzene (60 – 80) by continuous hot percolation using Soxhlet apparatus. This can be continued up to 24 hours. Now the solvent petroleum ether was extracted out and filtered and the Soxhlet is removed the obtained residue is stored in the dissector.

Chemicals :

- Streptozotocin.
- Glibenclamide
- Petroleum ether
- Ethanol
- Benzene
- Chloroform
- Studies were carried out in albino rats.

PHYTO CHEMICAL SCREENING.

The plant may be containing the following compound such as carbohydrate, protein, and lipids. That is utilized as food by man. It also contains the compound like. Tannins, glycosides, alkaloids. Volatiles oils. The compound that is responsible for lots of medicinal properties

TEST FOR CARBOHYDRATES

Molish test

The sample powdered was added with 1 ml of alpha naptool solution along with conc Sulphuric acid solution in the test tube reddish colour was produced at the junction between 2 liquid this is shows the presence of carbohydrate.

Fehling test.

To the sample powder was added with both Fehling A and Fehling B solution and placed in the water bath for a sufficient time. This shows the brick red colour. It shows the presence of carbohydrate.

Benedicts test.

To the sample powder add 8 drops of benedicts reagents and voil the sample vigorously for 5 min it shows the red ppt. this shows the presents of carbohydrate.

TEST FOR ALKALOIDS

To the small of stored powder (sample) was taken and add few drops of hydrochloric acid and filtered.

The filtered was tested with various alkaloid agents.,

Mayer's reagents:

To a small of above filter add small quantity of Mayer's reagent to form cream precipitate. This shows the presence of alkaloids.

Dragendorffs reagents

From the above filter add small amount of Dragendorffs reagents it forms a orange brown precipitate. This shows the presents of alkaloids.

TEST FOR FLAVONOIDS

To the filter of the plant extract add 5 ml of dilute ammonia solution and followed by the addition of concentrated sulphuric acid. It forms a yellow colour. It shows extract indicated the presence of flavonoids.

TEST FOR STEROIDS.

Salkowaski test

Few amount of plant extract was mixed with chloroform and the same volume of sulphuric acid is added on it. Cherry red colour was obtain in the chloroform layer. This shows the sample contain steroids.

Libbbermann burchatd test:

The extract is dissolved in 2 ml of chloroform 10 drops of acetic acid and conc. Sulphuric acid were added. Now the solution becomes reddish colour then it turns to bluish green colour. This shows the plant extraction indicates the presents of steroids.

TEST FOR TANNINS.

From few amount of plant extract is treated with vanillin hydrochloric acid reagent. It forms, pink or red colour due to the formation of phloroglucinol, it indicate the presence of tannins.

TEST FOR PROTEIN.

Mellon's reagents.

Mellon's reagents (mercuric nitrate in nitric acid containing a trace of nitrous acid) usually yields a white precipitate on addition to a protein solution which turns red on heating.

Ninhydrin Test.

From the sample solution add 2 drops a freshly prepared 0.2% ninhydrine reagent was added to the extract and heating. Development of blue colour may indicate the presence of peptide, amino acid (PROTEIN).

TEST FOR GLYCOSIDES:

Keller- killani test.

From the small quantity of small powder acetic acid was dissolved and adds few drops of ferric chloride and transferred to the surface of conc Sulphuric acid. At the junction, reddish brown colour was formed, which gradually becomes blue indicates the presents of cardiac glycosides.

TEST FOR SAPONINS.

<u>Foam test:</u>

1 ml of extract solution is diluted separately with distilled water to 20 ml and shaken in a graduated cylinder for 15 minutes. A 1 cm layer of foam indicates the presence of Saponins.

PHARMACOLOGICAL STUDIES.

ACUTE TOXICITY STUDIES.

Acute toxicity study was carried out in the albino rat on the petroleum ether extract of triumfetta rhomboidea plant leafs according to the OCED guidelines.

The healthy rats has been taken and divided into 4 different groups. Then the petroleum ether extract was dissolved in 0.6% if sodium carboxyl methyl cellulose on equal. All the four groups are named GROUP I, II, III, IV Accordingly. The drug has been administrated orally by the following ratio.

- GROUP I 1000 mg/kg.
- GROUP II 300 mg/kg
- GROUP III 50 mg/kg
- GROUP IV 5 mg/kg

The were monitored (general behavioral, neurological, autonomic, toxic effect and final for death after 24 hr) continuously for every 5 min and 10 min for every 1 hour. There was no morality and no signs of toxicity and no animal die even in higher dose of our drug (1000mg/kg). So the extracts were found to be safe at this dose level, and treated with higher dose of 2000mg/kg of body weight.

INDUCTION OF DIABETICS

Six adult albino rats weighting 250-300 grams (75-90 days old) were used for inducing diabetes. The animals were injected by Streptozotocin at the dose of **60 mg/kg** of the body weight intravenously. Streptozotocin induces diabetes within 3 days by destroying the beta cells. Diabetic animals and non-diabetic control group were kept in metabolic cages individually and separately and under feeding and metabolism control. Glucose in the blood of diabetic rats exceeded that of the non-diabetic control ones. Food consumption was measured in terms of (gr.), water consumption was measured in terms of (ml) and urine volume was measured in terms of (ml) on a daily basis while every 2-4 weeks in 80 days the levels of C-peptide, insulin and glucose in blood serum were also measured, so that chemical diabetes was verified in rats injected with Streptozotocin

ASSESSMENT OF DIABETIC.

Diabetic was conformed after 48 hr of streptozotocin injection, the blood samples were collected through retro orbital puncture and plasma glucose level were estimated by enzymatic GOD POD diagnostic kit method. The rat having fasting plasma glucose levels more than 250 mg/dL were selected and used for this study.

EVALUATION OF EXTRACT ON STREPTOZOTOCIN INDUCED DIABETIC RATS.

The albino rats on either sex have been selected for the experimental study. The weight of the should be around 170-240 gm. The animals are divided into six groups. Each group has 6 animals.

Group 1was kept as normal (normal rat) received only distilled water; group 2 was kept as negative control, Streptozotocin induced and received only water. Group 3 was treated with glibenclamide (10mg/kg)

Group 4, 5 and 6 is diabetic induced rat and treated with 100mg/kg,200mg/kg and 400mg/kg b.w of petroleum ether extract of *triumfetta rhomboidea.*

Table 2-Evaluation of extract on Streptozotocin induced diabetic Rats.

S no	Groups	Treatment
1	Group I	Normal control
2	Group II	Diabetic control
3	Group III	Diabetic + glibenclamide(10 mg/kg)
4	Group IV	Diabetic + Extract (100 mg/kg)
5	Group V	Diabetic + Extract (200 mg/kg)
6	Group VI	Diabetic + Extract (400 mg/kg)

Triumfetta rhomboidea. Extract was administered for 21 days at a two different dose levels 100, 200mg/kg of *Triumfetta rhomboidea.* Extract made in aqueous and given orally. The blood was collected by sinus orbital under the light diethyl ether anesthesia. The blood was centrifuged at 3000 rpm for 10 minutes. Body weight glucose was analyzed every week and lipid and lipoprotein profile from serum (TC, TG, HDL, LDL, VLDL.) were analyzed after 21 days.

OBSERVATION

Serum glucose level estimation (initial and final)

Body weight of the albino rats (initial and final)

ESTIMATION OF GLYCOSYLATED HEMOGLOBIN CONTENT

Glycosylated peptides are elevated several folds in diabetics. The use of the glycosylated hemoglobin (HbA1c) assay for long term diabetic monitoring of diabetic control is gaining much wider use and acceptance.

The hematological parameter glycosylated hemoglobin was determined by standard laboratory techniques.

ESTIMATION OF LIPIDS.

TOTAL CHOLESTEROL

The cholesterol in serum was estimated by using ecoline diagnostic kit. Cholesterol and its ester were released from lipoprotein by detergents cholesterol estrates hydrolyses the ester the sub subsequent enzymatic oxidation by cholesterol oxidize, Hydrogen peroxidase was formed. This was converted into colored quininemine in a reaction with 4-aminopyantipyrine and phenol catalyses by peroxidase the observance of the sample and of the standard was measured against the reagent blank value at 546nm. Cholesterol level in serum was expressed as mg/dL.

TRIGLYCERIDES.

The triglyceride level was estimated by using Ecoline diagnostic kit.

Triglyceride $\xrightarrow{\text{Lipase}}$ Glycerol + Fatty acid

Triglyceride $\xrightarrow{\text{GK}}$ Glycerol + Fatty acid

Glycerol 3 phosphate + O2 $\xrightarrow{\text{GPO}}$ Dihydroxy acetone phosphate+ H2O2

2H2O2 + Aminoantipyrine + 4 chlorophenol $\xrightarrow{\text{POD}}$ Chinonimine + 4H2O

The absorbance of the sample and of the standard was measured against reagent blank value at 546nm. Triglyceride level in serum was expressed as mg/dL.

HDL CHOLESTEROL

The cholesterol was separated from the serum after precipitation of LDL cholesterol by phosphotungstic acid precipitating reagent. The supernatant. After centrifugation was estimated using Ecoline diagnostic

kit. The absorbance of sample and of the standard was measures against the reagent blank value at 546 nm. HDL cholesterol level in serum was expressed as mg/dL.

LDL CHOLESTEROL.

The LDL Cholesterol is calculating by following formula

LDL Cholesterol = Total cholesterol – [HDL cholesterol – Triglyceride / 5].

LDL cholesterol level in the plasma is calculated and expressed in the unit of mg/dL.

VLDL CHOLESTEROL.

The VLDL Cholesterol is calculating by following formula

VLDL Cholesterol = Total cholesterol – HDL cholesterol – Triglyceride-LDL.

RESULT AND DISCUSSION.

Preliminary phyto chemical screening.

Triumfetta rhomboidea was subjected various chemical tested as per the standard methods for the identification of the various constituents. The result if this phyto chemical analysis is listed below.

Table-3 Qualitative phyto chemical screening of Triumfetta rhomboidea.

Plant constituent	Petroleum ether extract	Benzene extract	Ethanol extract	Chloroform extract.
Steroids	+	+	+	+
Carbohydrate	+	+	+	+
Flavonoids	+	+	+	-
Proteins and amino acids	-	-	-	-
Glycosides	+	+	-	+
Alkaloids	-	-	-	-
Saponins	+	-	+	+
Volatile oil	+	+	+	+
Tannins	+	+	+	+

"+" Presence, "-" Absence.

ACUTE TOXICITY STUDIES.

Acute toxicity studies on the albino rats show no morality at a dose of 2000mg/kg, during a time period of 14 days. During the study, no noticeable were seen in the rats. This help to predict that it does not contain any type of toxicity and it is full safe. So 100 mg/kg b.w ($1/20^{th}$ and 200mg/kg b.w ($1/0^{th}$) were selected of that dose for the further study.

Effect of *Triumfetta rhomboidea* on serum glucose levels

Streptozotocin treatment will produce significant increase in serum glucose level with respective normal control group. The administration of *triumfetta rhomboidea* extract 100mg/kg, 200 mg/kg and 400mg/kg and glibenclamide 10 mg/kg significantly reversed the increase in serum glucose concentration in Streptozotocin induced rats. The extract changes in the serum glucose level are shown in the table.

Effect of *Triumfetta rhomboidea* on body weight.

There was gradual increase in body weight in normal control while the diabetic control continues to lose the weight. However treated diabetic group gained 6.25%, 8.24% as compared with the diabetic control and diabetic treated towards normal range. Extract changes in the body weight shows in the table

Effect of *Triumfetta rhomboidea* on glycosylated hemoglobin.

There was a significant increases in glycosylated hemoglobin level is observed in diabetic rats. The level of glycosylated hemoglobin was decreased significantly in extract and glibenclamide treated rats compared to diabetic control rats. This can be shown in the table.

Effect of *Triumfetta rhomboidea* on serum lipid and lipoprotein.

STZ diabetic rats group were found to have significantly increased VLDL, LDL, TG, TC level and markedly decreased HDL levela as compared to normal control group. Treatment with *triumfetta rhomboidea* extract 100mg/kg, 200 mg/kg and 400mg/kg reduced significantly VLDL, LDL, TG, TC, levels

and markedly increased HDL level as compared to diabetic control groups. Positive control was significantly preventing the increasing the serum TC, TG, LDL, VLDL and decreasing the HDL level as compared to diabetic group. Thus the extract treatment restored all these changes near to normal value. This change in serum is listed on the table.

Table - 4 -Effect of Triumfetta rhomboidea extract on serum glucose level in normal control and STZ induced diabetic rats

S.NO	TREATMENT	SERUM GLUCOSE LEVEL	
		Initial	Final
1.	Normal control	90.97±1.47	89.52±2.16
2	Diabetic control	259.3±3.51	405.3±1.265
3.	Diabetic+ Glibenclamide 10mg/kg	267.8±3.15	129.5±1.035
4.	Diabetic+ Extract 100mg/kg	238.0±2.65	325.2±2.46
5.	Diabetic+ Extract 200mg/kg	241.9±1.25	224.2±2.49
6.	Diabetic+ Extract 400mg/kg	242.1±3.21	140.2±3.19

All values are expressed in MEAN ± SEM (n=6)

Table -5-Effect of Triumfetta rhomboidea extract on body weight in normal control and STZ induced diabetic rats.

s/no	TREATMENT	BODY WEIGHT	
		Initial	Final
1.	Normal control	241.9±3.51	275±1.95
2.	Diabetic control	248.9±1.43	190±1.64
3.	Diabetic + Glibenclamide.	243.5±1.53	275.8±1.65
4.	Diabetic+ Extract 100	243.2±2.51	282.8±2.76
5.	Diabetic+ Extract 200	250.5±3.23	301.2±2.82
6.	Diabetic + Extract 400	241.6±3.84	261.1±1.44

All value are expressed mean ±SEM (n=6)

P<0.001, as compared to diabetic control

P<0.001 as compared to Normal control.

Table in parenthesis indicate % fall in body weight as compared to initial value.

Table -6-Effect of Triumfetta rhomboidea extract on serum lipid and lipoprotein profile in normal control and STZ induced diabetic rats.

S.NO	Treatment	TC(mg/Dl)	TG(mg/Dl)	HDL(mg/Dl)	LDL(mg/Dl)	VLDL (mg/Dl)
1.	Normal control	88.6±4.54	60.01±1.6	41.5±1.32	92.5±1.07	26.5±1.32
2.	Diabetic control	231±7.45	131±4.21	21.3±1.42	131±1.67	52.3±2.18
3.	Diabetic + Glibenclamide (10mg/kg)	141±2.35	101±2.90	45.6±1.48	102±2.06	35.2±1.65
4	Diabetic + extract (100mg)	136±3.95	116±2.62	48.3±2.01	113.±2.62	41.3±1.56
5.	Diabetic + extract (200mg)	132±3.52	112±3.01	45.4±1.30	102±2.12	39.1±2.06
6.	Diabetic + extract (400mg)	89.3±1.03	62.3±3.65	39.3±1.37	98.6±1.68	23.71±2.18

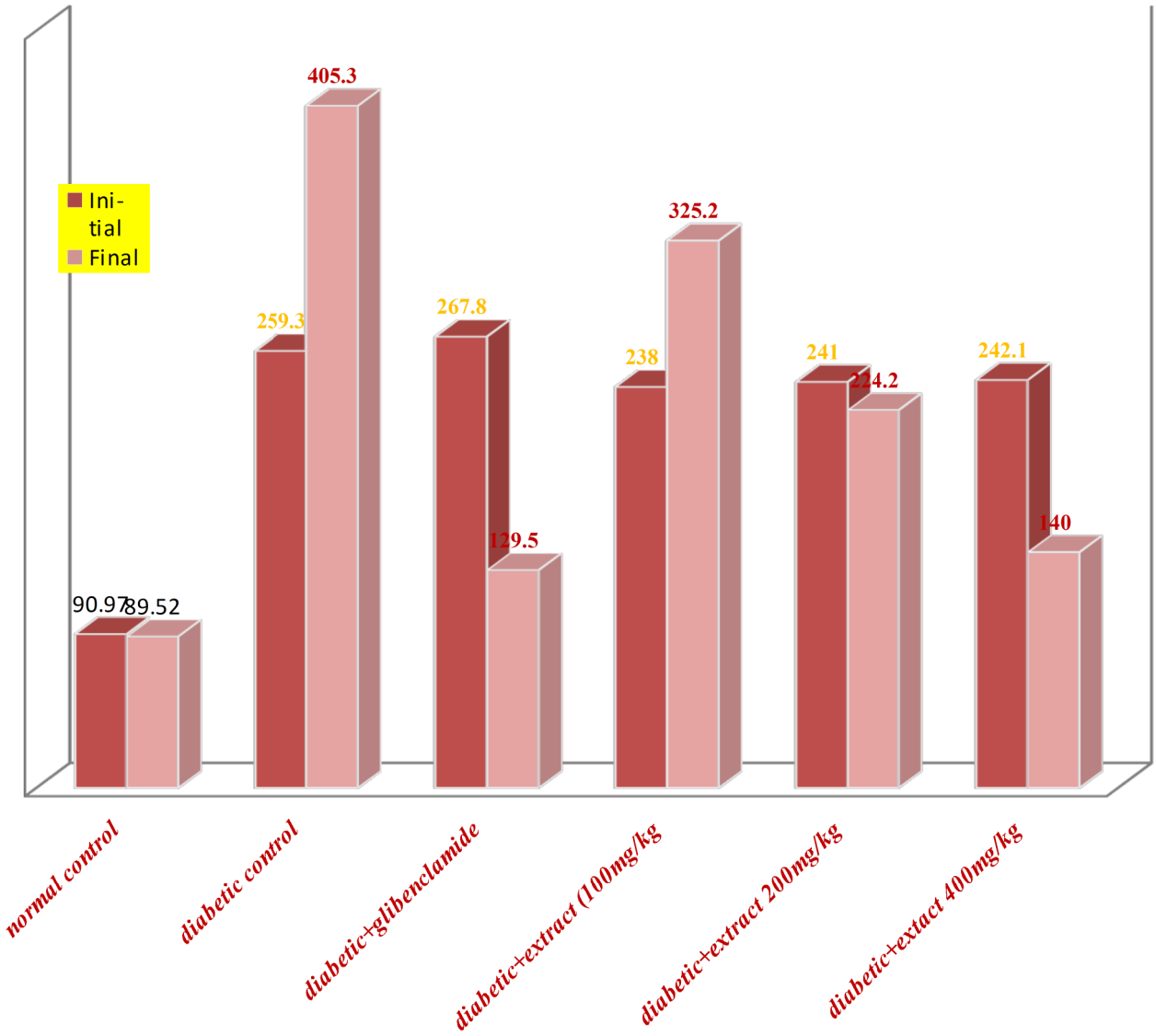
All value are expressed as mean ±SEM (n=6)

P<0.001, as compared to diabetic control

P<0.001 as compared to Normal control.

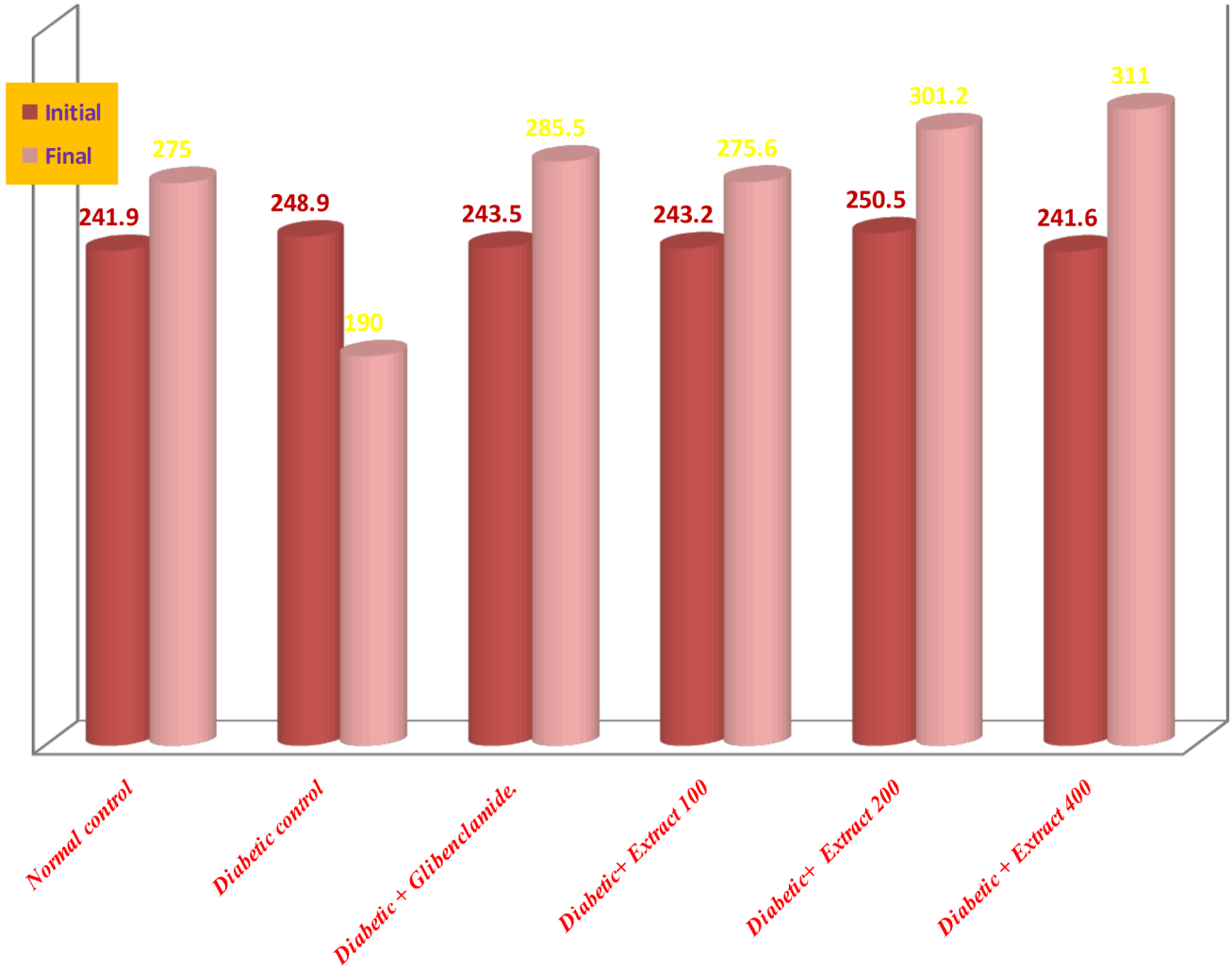
Table in parenthesis indicate % fall in body weight as compared to initial value.

Serum glucose level

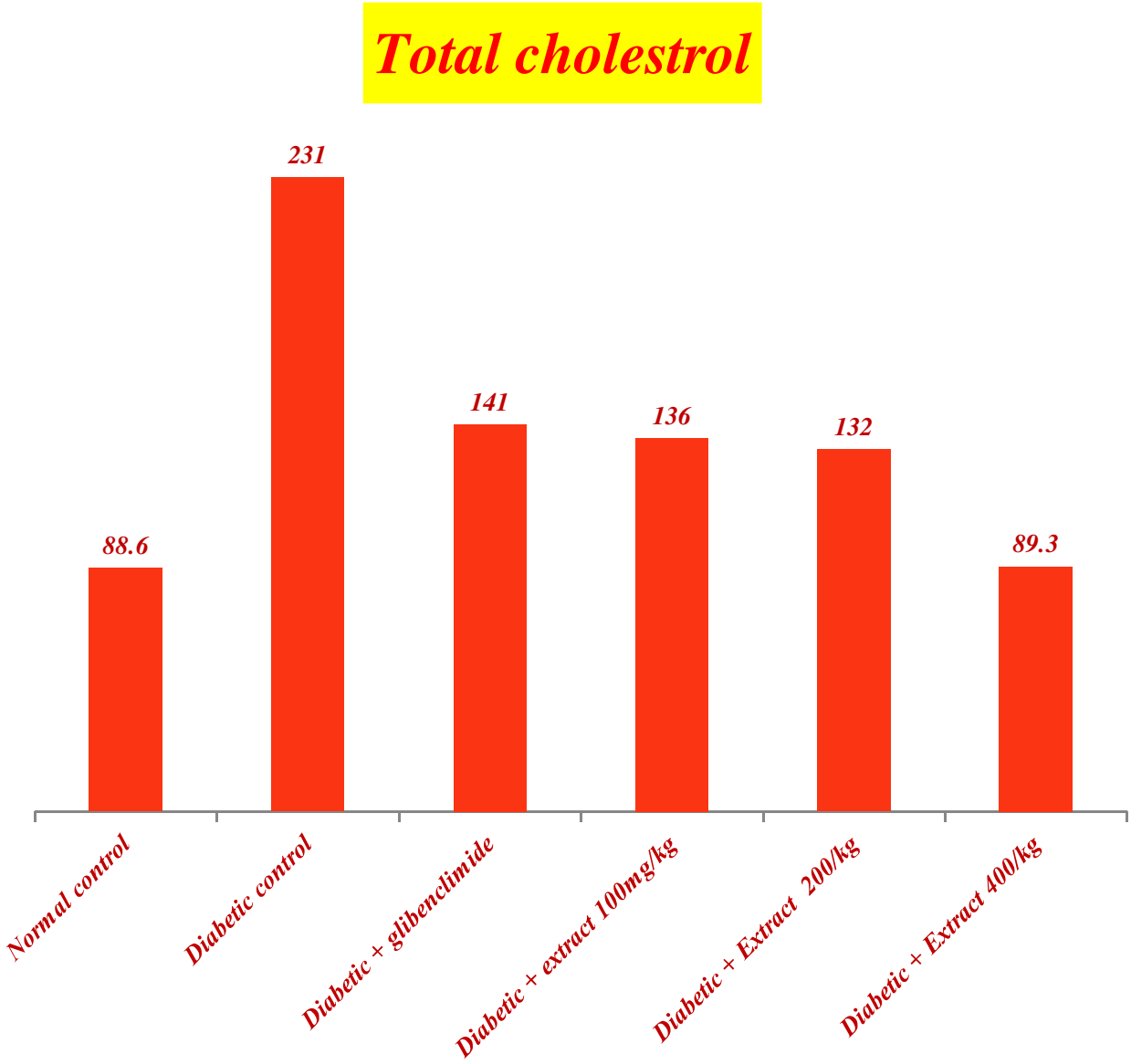


The Figure showed of Triumfetta rhomboidea extract serum glucose level in normal control and STZ induced diabetic rat. Values are expressed as mean ± SEM of 6 animals in each group.

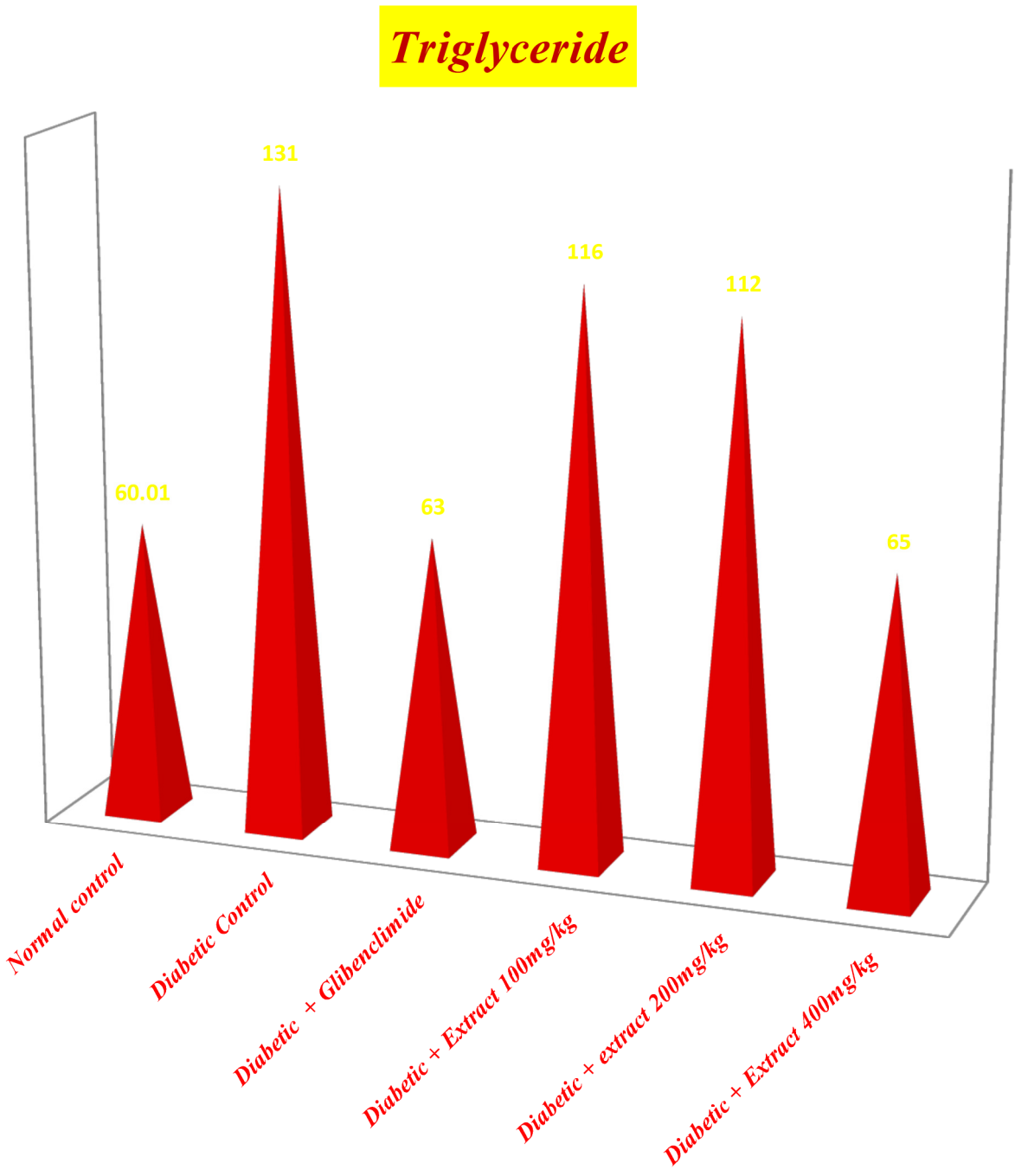
Body weight of the animal



The Figure showed of *Triumfetta rhomboidea* extract on Body weight in normal control and STZ induced diabetic rat. Values are expressed as mean ± SEM of 6 animals in each group

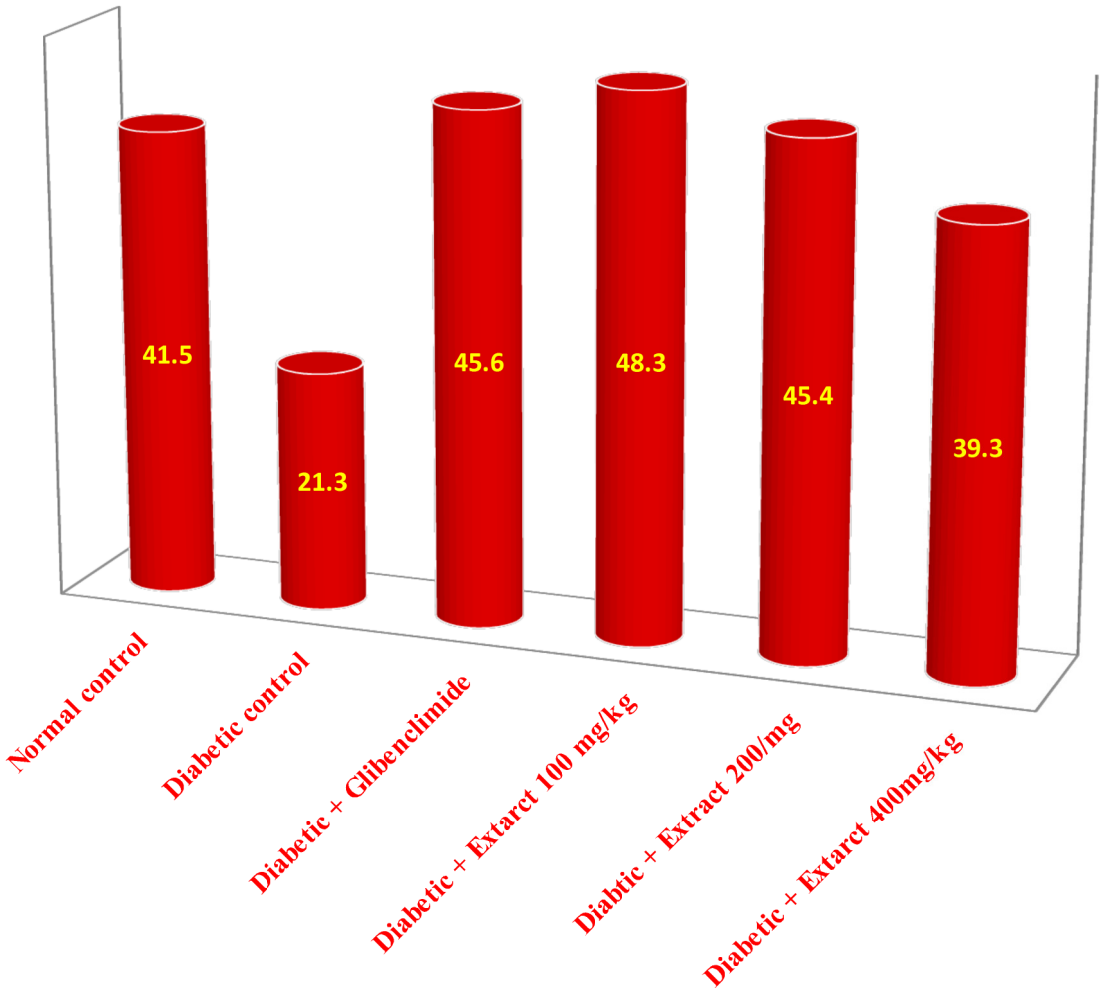


The Figure showed of Triumfetta rhomboidea extract on total cholesterol in normal control and STZ induced diabetic rat. Values are expressed as mean ± SEM of 6 animals in each group



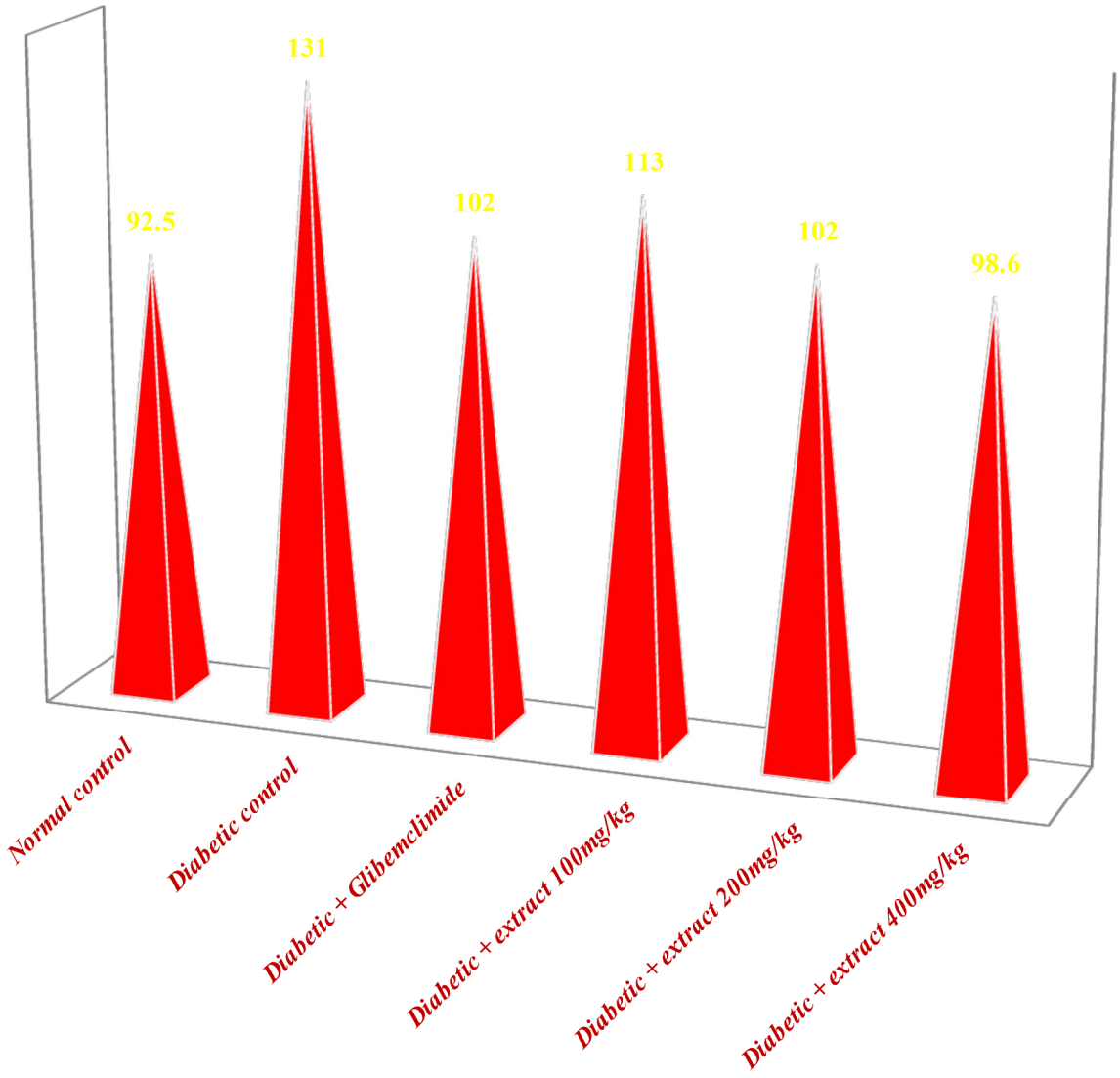
The Figure showed of Triumfetta rhomboidea extract on triglycerides in normal control and STZ induced diabetic rat. Values are expressed as mean ± SEM of 6 animals in each group

High Density Lipids.

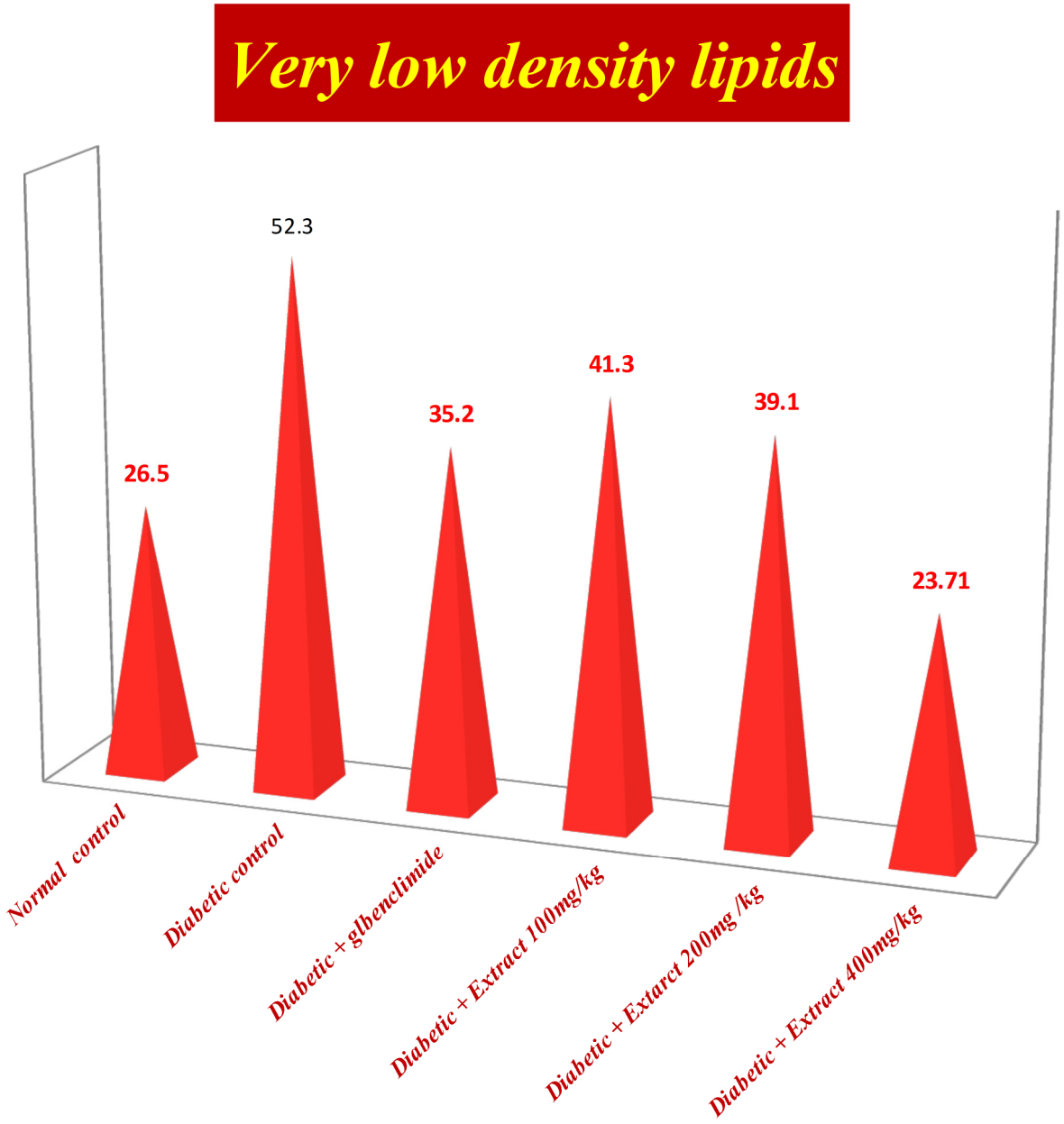


The Figure showed of Triumfetta rhomboidea extract on High density lipids in normal control and STZ induced diabetic rat. Values are expressed as mean ± SEM of 6 animals in each group

Low density lipids



The Figure showed of Triumfetta rhomboidea extract on low density lipids in normal control and STZ induced diabetic rat. Values are expressed as mean ± SEM of 6 animals in each group



The Figure showed of Triumfetta rhomboidea extract on very low density lipids in normal control and STZ induced diabetic rat. Values are expressed as mean ± SEM of 6 animals in each group.

DISCUSSION

Diabetes is a common chronic ailment for which the patient has to take insulin to maintain the blood sugar level. It is interesting to see how the triumfetta rhomboidea extract tackles this problem. It corrects the function of pancreas, stimulating it to produce insulin in the natural way, which in turns way, which I turn maintain the blood sugar level. Triumfetta rhomboidea revitalizes and rejuvenates the organs, the dysfunction of which is causing the disease. This bring back normal functioning of the organs. It is also maintaining the healthy state body. Since no artificial chemical are involved, it doesn't cause any side effects

Qualitative Phytochemical screening and ethno botanical survey on the triumfetta rhomboidea are vaulted the presented of certain phyto constitutions such alkaloids, tannins, carbohydrates, glycosides, protein and amino acids, phytosterol, high amount of terpeniods

The phyto chemical constituents such as glycosides, tannins, triterpenoids, flavonoids, alkaloids may be linked to the anti diabetic activity.

To check the safety profile of the triumfetta rhomboidea extract it was subjected to the acute toxicity study which conformed the absence of any toxicity or mortality at the higher dose of 2000mg/kg. Thus the triumfetta rhomboidea extract can be classified as a safe drug category according to the Global harmonized Classification System quoted in the OECD guidelines 1996.

Based on the articles toxicity studies two dose level were selected for the evolution of various pharmacological studies properties (100,200and 400mg/kg).

Diabetic mellitus (DM) is an endocrine disorder in which the glucose metabolism is impaired because of total loss of insulin after destruction of pancreatic beta cells or because of inadequate release of insulin from the pancreatic cells of beta cells. The fundamental mechanism underlying hyperglycemia involved over population and decreases utilization of glucose by

the tissue. In the presence study was observed that whether the triumfetta rhomboidea extract have the effect of lipid profile, anti oxidant system or not and in addition to its antihyperglycaemic action of STZ induced diabetic in albino rats

Streptozotocin a beta cytotoxin induces diabetic in a wide variety of animal species including rats by selectively damaging the insulin secreting beta cells of pancreas i.p injection of STZ produces fragmentation of DNA of beta cells of pancreas which stimulates poly (ADP ribose and deflects NDA ultimately leading of destruction of beta cells and it is evidenced by clinical symptoms of hyperglycemia.

Dose dependant of the effect of the glibenclamide showed rapid normalization of blood glucose due to its insulin releasing effects.

In our present study there was a significant weight gain triumfetta rhomboidea treated the diabetic rats compared with the normal control rats and this observation shows anabolic effect of the triumfetta rhomboidea extract on body weight on the diabetic rats.

Hyperglycemia and insulin resistance both seem to have important in the pathogenesis of macro vascular complications. Diabetes mellitus causes a disturbance in the uptake of glucose as well as glucose metabolism. The hyperglycemia in the diabetes might inhibit tissue repair in the macro vascular beds. In the present study of triumfetta rhomboidea extract treated group shows hypoglycemic activity and it confirms the presence of the anti- diabetic activity.3

Sulfonylurea such as glibenclamide is often used as a standard drug in the STZ induced diabetic to compare to the efficacy of antihyperglycaemic compound. In study there was a significant elevation in blood glucose level in the diabetic control group as compared with normal animal. The triumfetta rhomboidea extract treated group exhibited significant reduction of fasting plasma glucose

level as compared to the diabetic control group. Over production of glucose by means excessive hepatic glycogenolysis and gluconeogenesis is one of the fundamental basis of hyperglycemia in diabetes mellitus.

Increased glycation of protein has been found to be consequence of diabetic complication. A number of proteins including hemoglobin are Glycated to a greater degree in diabetic glycosylated hemoglobin (HbA1c) is the measurement of the mean blood glucose level over the previous 6-8 weeks, during the life span of RBC. It has been shown to be an important parameter of chronic glycameic control in patient with diabetic mellitus (DM), an elevated HbA1c almost always indicted DM. in our present study glycation of protein is significantly lowered by the treatment with triumfetta rhomboidea extract.

The most common observed lipid abnormalities in diabetics are hypertriglyceridemia and hypercholesterolemia. A marked increase in total cholesterol and decrease in HDL cholesterol have been observed in diabetics control rats. Insulin deficiency results in failure to activate the lipoprotein lipase thereby causing hypertriglyceridemia. There was a significant control of the level of serum lipids in triumfetta rhomboidea extract treated diabetic rats. In diabetes, LDL carries cholesterol to the peripheral tissue where it is deposited, where HDL transports cholesterol from peripheral tissue to the liver and this aids its excretion. Hence increase in LDL is atherogenic. In our present study, there was a significant decrease in triglyceride LDL and T.C levels, where as there was a significant increase in the HDL level.

SUMMARY AND CONCLUSION

The presented study is an attempt to investigate the effect of petroleum ether extract of triumfetta rhomboidea on Streptozotocin induced diabetic in albino rats.

The Phytochemical study was screening showed the presence of tannins, carbohydrate, Flavonoids, alkaloids, reducing sugar and amino acid which is responsible for the anti diabetic activity.

The animals were induced with STZ at a dose of 55mg/kg intraperatoneal and the diabetic animals were treated with triumfetta rhomboidea extract (100, 200, 400mg/kg) for 21 days orally. The serum glucose, body weight lipid profile, liver glycogen were measured from the pancreas homogenate were measured which showed significant activity.

The finding of the presence investigation suggests the triumfetta rhomboidea extract has potential for its evaluation as protective agents against toxicity induced by Streptozotocin.

Clinical assessments of triumfetta rhomboidea extract determination of underlying mechanism of the protective effects in interesting topics requiring further study

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COMMITEE FOR THE PURPOSE OF CONTROL AND SUPERVISON OF EXPRIMENT ON ANIMAL.

Reg:

Ref No: IAE 1012/c/06/CPCSEA-Corres-2013-2014

21.06.2013

Sub: Approval of animal studies – project submitted for clearance –Resolution passed by Institutional Animal Ethical Committee held 21st June 2013

Sir,

With reference to the subject cited above, please find the enclosed list of project cleared for the animal studies by the institutional animal committee of RVS College of Pharmaceutical Science, in its meeting held on 21st June 2013 at the college premises.

Dr.D.Benito Johnson
Secretary Member
IAEC

Dr .R. Venkatanarayanan
Principal/Chairman IAEC

No. of resolution Passed -55.

Resolution No: 55

It is resolved to pass the clearance for the animal study of the project **"Anti diabetic activity of *Triumfetta rhomboidea* on streptozotocin induced diabetic in albino rats"** submitted by **Padma Vinayaka Moorthy.R** Department of pharmacology, RVS College of pharmaceutical Science, Sulur, Coimbatore- 641 402,Tamilnadu.